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INSIDE

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I Can't Get No Salivation

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD, MA

Chair, Department of Integrative Medicine, Ross University School of Medicine, Commonwealth of Dominica

Dr. Wilke reports no financial relationship to this field of study.

Synopsis: *Elders who ate sorbet before a meal ate more of the rest of their meal.*

Source: Crogan NL. Managing xerostomia in nursing homes: Pilot testing of the Sorbet Increases Salivation intervention. *J Am Med Dir Assoc* 2011;12:212-216.

Xerostomia (dry mouth) is one of several contributors to malnutrition in the elderly.[1] This pilot study from the University of Arizona's Center on Aging hypothesized that individuals suffering from xerostomia could stimulate salivation by consuming lemon-lime sorbet and that, subsequently, they would increase their food intake.

The study was conducted at a skilled nursing facility. Participants were residents who were taking ≥ 4 medications known to cause xerostomia and who met the following inclusion criteria: age ≥ 65 years, Mini Mental State Examination score ≥ 12, taking meals in the main dining room, and screened positive for xerostomia. Residents who were receiving palliative or hospice care, who had received head or neck radiotherapy, who had salivary gland surgery, or who had Sjögren syndrome were excluded. To confirm the presence of xerostomia, the subjects underwent a Modified Schirmer Test. This involves measuring saliva output with strips of filter paper, performed at baseline, and then three more times at 1-minute intervals after consuming water or sorbet. Sorbet, on average, produced more saliva than water.

Twenty residents were randomly selected; 12 agreed to participate, 8 female and 4 male. Two did not complete the study secondary to hospitalization. The study was conducted over 12 weeks. Each sub-

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ject was given 2 ounces of sugar-free sorbet before lunch for two 3-week periods divided by a 6-week no-treatment period. (Patients with xerostomia are at high-risk for severe dental decay; hence, the use of a sugar-free sorbet.) Their lunch plates, filled with food, were weighed before serving and again after the meal to measure the amount of food consumed. Nine of the 10 residents ate more food during the sorbet weeks than the non-sorbet weeks, but in only one resident did the difference reach statistical significance. In that patient, the difference in weight of food eaten was about 7 grams.

■ COMMENTARY

This is a very small study and not robust enough to draw any conclusions, but the intervention is so simple and appealing, we should pay attention to it. It is low-cost and would be easy to implement. Anything that confirms the wisdom of "Life is short; eat dessert first" is okay in my book, but "more food eaten" falls short of my desires for a primary endpoint. What about improved health status, or, at the very least, improved quality of life? A larger, more vigorous study should be undertaken.

Sorbet is simply a frozen sweetened water, pureed fruit, or juice concoction often served before the main course of a meal to cleanse the palate. I wonder if fruit other than lemons and limes would work as well, and whether sherbet (fruit and milk) would have a similar effect.

Xerostomia interferes with proper nutrition by diminishing the taste of food and making chewing and swallowing difficult. It usually is treated by correcting the underlying cause, or, when that is not possible, by sipping water frequently, eating ice chips, stimulating salivation, or replacing it with artificial saliva preparations containing hypromellose or methylcellulose. Sucking on sugar-free lozenges or candy, chewing gum, or administering pilocarpine or cevimeline can stimulate salivary flow, but those drugs have their own set of adverse effects.[2]

As interesting and potentially useful as this intervention could be, it begs the questions: Why were all of these patients on at least four drugs known to cause xerostomia? Shouldn't the first step be to do a diligent medication review and trim the list? Although there are several causes of xerostomia (e.g., radiation treatment of head and neck cancer, Sjögren syndrome, Parkinsonism, AIDS, and diabetes), most often it is the result of the drugs that we prescribe. Drugs that cause xerostomia are usually anticholingerics or antimuscarinics, although there are others (e.g., diuretics and benzodiazepines). These drugs have other unintended consequences.[3] The mantra in the elderly should be "less is more." The fact that we can prescribe medication shouldn't compel us to do so. ■

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Desperate Diseases Call for Drastic Diets

ABSTRACT & COMMENTARY

By Barbara A. Phillips, MD, MSPH

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Dr. Phillips serves on the speakers bureaus for Cephalon, Resmed, and Respironics.

Synopsis: *A very low energy diet followed by a weight maintenance program results in significant improvements in weight, obstructive sleep apnea, metabolic factors, and quality for at least a year.*

Source: Johansson K, et al. Longer term effects of very low energy diet on obstructive sleep apnea in cohort derived from randomised controlled trial: Prospective observational follow-up study. *BMJ* 2011;342:d3017.

This report is an extension of a shorter-term study conducted to assess the effects of a very low energy (or calorie) diet on obstructive sleep apnea. The study was conducted at the Obesity Unit at Karolinska University Hospital in Sweden. The participants were all obese men with moderate-to-severe obstructive sleep apnea who were stable on continuous positive airway pressure (CPAP). Patients were randomized to a very low energy diet or a control group for the first 9 weeks, but then the control group was also started on the very low calorie diet after 9 weeks as a control group. After a 9-week very low energy diet period, both groups entered a weight loss maintenance program. Since the control group was only a control for the first 9 weeks, data from both groups were pooled for this 1-year follow-up analysis.

The very low energy weight loss diet was a 2.3 MJ/day (about 550 calories) liquid energy intake protocol (Cambridge Weight Plan, Northants, UK) for 7 weeks, followed by 2 weeks' gradual introduction of normal food to reach 6.3 MJ/day (about 1500 calories) at week 9. Patients were also scheduled for six visits with clinical examinations and group sessions. The maintenance program started right after the very low energy diet period and was essentially behavior modification group therapy supplemented with a self-help manual. Each group included 13-15 patients and was led by a research nurse and a dietitian. Each patient also was seen by a nurse for anthropometry measurements and a dietitian for individual dietary advice.

The protocol specified use of partial meal replacement as a first option (exchanging one or two daily meals with an approximately 140 calorie meal replacement) if the patient's weight had increased by more than 2 kg since the last visit. (Of note, almost all [86%] the participants reported using partial meal replacement at least once). The secondary option was sibutramine or orlistat prescription, but orlistat was prescribed to only one patient.

Of the original 63 patients in the study, 49 completed sleep and adiposity follow-up measures (this included five people who dropped out of the weight maintenance program but were willing to follow-up), and 44 completed a full year of treatment.

At baseline, the majority of patients had severe obstructive sleep apnea, metabolic syndrome, hypertension, and dyslipidemia. Slightly more than half were obese; 56%, 41%, and 3% had BMIs of 30-34.9, 35-39.9, and ≥ 40, respectively. Their physical quality-of-life component was lower than in the general male Swedish population while the mental component was similar.

During the very low energy diet and full treatment program, weight, BMI, waist circumference, neck circumference, and percentage body fat all decreased significantly, but all these variables increased significantly during the weight maintenance period. Of the participants analyzed at the 1-year follow-up, one was normal weight (BMI < 25), 27 were overweight, and 35 (56%) remained obese (BMI ≥ 30).

All sleep variables improved significantly after the very low energy diet period and full treatment program, but then worsened significantly during the weight maintenance period. However, neither the weight nor the sleep-disordered breathing returned to baseline severity during 1 year of follow-up. Overall, the apnea-hypopnea index (AHI) fell by 58% after 9 weeks of a very low energy diet and was still statistically and clinically reduced (by 47%) at 1 year. At the 1-year follow-up, six patients (10%) had total remission of obstructive sleep apnea and 30 (48%) patients no longer required CPAP (23 of these did not need any further treatment and 7 shifted to treatment with an oral appliance). Improvements in the AHI were larger in those men with severe obstructive sleep apnea at baseline than in those with moderate disease. Patients who lost ≥ 15 kg had larger improvements in the AHI at 1 year than patients who lost less, but even modest weight loss resulted in significant improvement in AHI.

Between baseline and 1-year follow-up, the physical component of the quality-of-life score had increased by 4 units (2 to 6; $P < 0.001$) and was similar to that in the general population. Between baseline and 1-year follow-up all measured metabolic variables improved significantly. Dyslipidemia disappeared in 11/59, insulin resistance in 10/20, and metabolic syndrome in 23/44. Of those with hypertension at baseline, resolution occurred in 8/36 (22%).

During the very low energy diet period, 13 patients had an adverse event classified as probably causally linked with the very low energy diet, including constipation (n = 3), increased alanine aminotransferase activity (n = 6), dizziness (n = 1), gout (n = 2), and dry lips (n = 1). All adverse events had disappeared by the visit 2 weeks after the very low energy diet period. During weight loss maintenance there were five additional adverse events probably causally linked to treatment with very low energy diet, including gallstones (n = 3), gout (n = 1), and kidney stones (n = 1). No patient discontinued treatment because of adverse events.

■ COMMENTARY

Obstructive sleep apnea has roughly the same prevalence as asthma,[1] but is arguably more of a public health risk because it is associated not only with increased cardiovascular risk, but also with increased risk of moving vehicle crash.[2-4] CPAP treatment is effective, but CPAP adherence — while no worse than for any other medical treatment — is not optimum. The origi-

nal report of this cohort[5] covered only 9 weeks of treatment, and the subjects were already regaining weight at the end of the first follow-up period after they left the very low energy diet and went to the maintenance program. I was among many skeptics who believed that neither the weight loss nor the improvement in sleep apnea would persist over time. This report has proved me wrong — though there were dropouts and failures, as a whole, the patients had significant, persistent improvements not only in weight and sleep apnea, but also in metabolic factors and quality of life.

Indeed, while reading this report, I kept contrasting this approach to that of upper airway surgery such as uvulopalatopharyngoplasty (UPPP). UPPP has about the same short-term "cure" rate as is reported here (50%), but we don't know very much about its effects on blood pressure, metabolic factors, and quality of life. Indeed, long-term follow-up of those who undergo UPPP is uncommon, but we do know that relapse occurs, mostly related to weight gain.[6] The weight loss protocol in this study was extensive and labor-intensive, but almost certainly cheaper than surgery. And the adverse events (dry lips, gallstones) for the very low calorie approach pale in comparison to those related to UPPP (speech change, palatal stenosis, and, er, death).

Talking to patients about weight loss is hard. Getting them into programs is even harder. But this report suggests that it can really make a difference. One of my favorite lines in clinic is, "You are a smart person, and you have struggled with this for a long time. If you were going to lose weight on your own, you would have done it by now. Let's get some help." ■

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Proton Pump Inhibitors and Clopidogrel

ABSTRACT & COMMENTARY

By Harold L. Karpman, MD, FACC, FACP

Clinical Professor of Medicine, UCLA School of Medicine

Dr. Karpman serves on the speakers bureau for Forest Laboratories.

Synopsis: *Proton pump inhibitor use in clopidogrel-treated post-percutaneous coronary intervention patients was not associated with an increased risk of all-cause death, nonfatal myocardial infarction, repeat revascularization, or major adverse cardiovascular events.*

Source: Banerjee S, et al. Effect of concomitant use of clopidogrel and proton pump inhibitors after percutaneous coronary intervention. *Am J Cardiol* 2011;107:871-878.

Dual antiplatelet therapy with aspirin and clopidogrel has been accepted as the most appropriate treatment for patients with acute coronary syndromes (ACS) who have received percutaneous coronary intervention (PCI) therapy.[1] The increased risk of gastrointestinal bleeding due to aspirin/clopidogrel therapy[2] has been significantly reduced because of the use of proton pump inhibitors (PPI)[3]; however, since both clopidogrel activation and PPI metabolism have a common metabolic pathway via the hepatic cytochrome P450 isoenzymes, PPI administration to patients receiving clopidogrel has the potential of reducing blood levels of the pharmacologically active clopidogrel metabolite thereby attenuating the effects of the drug on platelet aggregation.[4] Most observational studies have reported adverse effects in patients receiving both drugs, although these concerns have not been supported by analyses from randomized clinical trials.[5-8]

Because only a few previous studies have addressed the effects of PPI administration on platelet aggregation in patients receiving clopidogrel therapy who have been subjected to PCI, Banerjee and his colleagues analyzed the clinical outcomes of 23,200 post-PCI patients who were taking these drugs. They concluded that use of PPIs in clopidogrel-treated post-PCI patients with coronary stent implantations was not associated with an increased risk of all-cause death, nonfatal myocardial infarction, repeat revascularization, and/or major adverse cardiovascular events after controlling for the possible confounding effects of angina misdiagnosis in these patients presenting to Veteran Administration hospitals with upper abdominal or lower chest complaints.[9-11]

■ COMMENTARY

The findings from the Banerjee study[9] simply have re-emphasized the potential diagnostic challenge of differentiating ischemic symptoms in patients presenting to the hospital with chest or upper abdominal complaints.[10-12] When treating a patient with chest pain and/or upper abdominal complaints, a significant potential exists that PPIs will be prescribed for a presumptive diagnosis of gastroesophageal reflux disease when, in fact, the symptoms were actually due to cardiac ischemia.[10] Although the prevalence of confirmed ischemic heart disease in all patients presenting with gastroesophageal reflux disease-like symptoms is extremely low, in the range of 0.4%,[10] its prevalence in patients after PCI and coronary stent implantation had not been previously systematically analyzed until the Banerjee study.[9] Unknown confounders must be taken into account, for example, all of the data analyzed in the Banerjee study were obtained from the national Veterans Affairs Pharmacy Benefits Management database, which could have possibly been influenced by the consistency and duration of clopidogrel and PPI exposure patterns that was derived solely from the pharmacy prescription refill data. Of course, the weak link in any conclusions from data obtained from prescription refills is in large part significantly influenced by patient compliance and/or noncompliance from the prescribed drugs' dosing schedules.

In any case, PPI use in patients receiving clopidogrel appears to be safe in those who are post-PCI with coronary stent implantation but the jury still appears to be out for patients who are receiving the two drugs after other cardiovascular events. Careful clinical evaluation of all patients who are receiving both drugs is clearly indicated in an attempt to determine whether recurrent chest symptoms are secondary to angina pectoris or possibly due to upper gastrointestinal disease — if the distinction cannot be made or if recurrent symptoms are determined to be secondary to angina, consideration of withholding or discontinuation of PPI drug therapy should probably be entertained until the results of further studies have become available. ■

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Pharmacology Update

Telaprevir Film-Coated Tablets (Incivek™)

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; and Assistant Professor of Medicine, University of California, San Francisco. Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.

Drs. Elliott and Chan report no financial relationship relevant to this field of study.

A second NS3/4A protease inhibitor has been approved by the FDA for the treatment of chronic hepatitis C (HCV) genotype 1, joining the recently approved boceprevir (Victrelis™). Telaprevir is marketed by Vertex Pharmaceuticals as Incivek.

Indications

Telaprevir is indicated, in combination with peginterferon and ribavirin, for the treatment of genotype 1 chronic hepatitis C in adult patients.[1] This includes treatment-naïve patients, those with compensated liver disease including cirrhosis, or those who are treatment-experienced with interferon-based treatment. The latter group may be relapsers, partial responders, or null responders.

Dosage

The recommended dose for treatment-naïve and prior relapsers is 750 mg (two 375 mg tablets) taken three times a day (7-9 hours apart) with food.[1] Telaprevir should be taken with peginterferon and ribavirin (triple therapy) for 12 weeks followed by a response-guided regimen.[1] If virus is undetectable at week 4 and 12, peginterferon/ribavirin (PR) therapy is continued for an additional 12 weeks. If virus is detected at week 12, an additional 36 weeks of PR therapy is recommended. For prior partial or null responders, 36 weeks of dual therapy is recommended after 12 weeks of triple therapy. Treatment should be discontinued if HCV-RNA is equal to or greater than 1000 IU/mL at treatment week 4 or 12, or detectable at treatment week 24.

Telaprevir is available as 375 mg tablets.

Potential Advantages

The addition of telaprevir to peginterferon alfa-2a/ribavirin significantly improved sustained virologic response (SVR) compared to peginterferon/ribavirin alone in both treatment-naïve and previously treated patients with chronic hepatitis C genotype 1.[1,2]

Potential Disadvantages

Most common adverse events associated with telaprevir (compared to peginterferon/ribavirin) are rash (56% vs 34%), pruritus (47% vs 28%), nausea (39% vs 28%), anemia (36% vs 17%), and diarrhea (26% vs 17%).[1] Telaprevir is an inhibitor of CYP3A and p-glycoprotein. Concomitant administration with drugs that are metabolized by CYP3A or substrates of p-glycoprotein may increase the plasma levels of these drugs.

Comments

The safety and efficacy of telaprevir was evaluated in three randomized clinical trials (ADVANCE, ILLUMINATE, and REALIZE).[1,2] In ADVANCE, treatment-naïve patients were randomized to telaprevir for 12 weeks (T12PR) (n = 363) or 8 weeks plus 4 weeks of placebo (T8PR) (n = 364) in combination with peginterferon alfa-2a (180 mcg/week) and ribavirin (800 mg/day or 1200 mg/day based on whether weight was equal to or less than or greater than 75 kg) followed by PR for 24 or 48 weeks. Patients who achieved undetectable virus at weeks 4 and 12 received 24 weeks of therapy and those with detectable virus received 48 weeks. The control group was peginterferon/ribavirin for 48 weeks (PR48) (n = 361). The primary efficacy endpoint was SVR, defined as HCV-RNA less than 25 IU/mL at 24 weeks after the planned end of treatment. SVR rates were 75% for T12PR, 69% for T8PR, and 44% for PR48. Most common adverse events were fatigue, pruritus, nausea, anemia, and headache.

ILLUMINATE was designed to evaluate whether it was beneficial to extend therapy from 24 to 48 weeks in patients who had achieved undetectable virus at weeks 4 and 12 weeks. SVR rates were 92% (149/162) for T12/PR24 and 88% (140/160) for T12/PR48. Relapse rates were 5.7% (9/159) and 1.9% (3/154), respectively.[3] The findings suggest no real overall added advantage with 48 weeks of therapy.[1-3] However, a small subset of patients with cirrhosis achieved a higher SVR with 48 weeks of therapy 92% (11/12) compared to 67% (12/18).

REALIZE included patients who were partial or null responders or relapsers. These patients were randomized 2:2:1 to: 1) 12 weeks of telaprevir with PR, 4 weeks of placebo plus PR, and 32 weeks of PR (T12PR48); 2) 4-week lead-in with PR followed by 12 weeks of telaprevir plus PR, and PR for 32 weeks; or 3) PR for 48 weeks. The overall SVR rates for telaprevir/PR were 86% for prior relapsers, 59% for prior partial responders, and 32% for prior null responders compared to 22%, 15%, and 5% for PR only. Relapse rates for telaprevir were 24% for prior null responders, 20% for partial responders, and 3% for prior relapsers. Skin reactions (rash and pruritus) and anemia were more likely associated with telaprevir compared to peginterferon/ribavirin.

Clinical Implications

Telaprevir is the second protease inhibitor approved for the treatment of HCV genotype 1 infection. Both boceprevir and telaprevir have improved SVR by roughly 60% to 70% compared to peginteferon and ribavirin

alone. There are no direct comparisons between telaprevir and boceprevir. In addition, telaprevir is combined with peginterfon alpha-2a while boceprevir was used with peginterferon alpha-2b, doses of ribavirin were slightly different, and treatment schedules differ. Initial selection may be based on simplicity of the dosing schedule and cost. ■

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CME Questions

32. In the pilot study using sugar-free sorbet to treat xerostomia, which statement is true?
a. Sorbet produced less saliva than water.
b. Most subjects ate less food during the sorbet weeks than the non-sorbet weeks.
c. Participants were taking ≥ 4 medications known to cause xerostomia.
d. Participants gained weight during the sorbet weeks, but not the non-sorbet weeks.

33. For obese patients with obstructive sleep apnea, a very low energy diet followed by a weight maintenance program for 1 year:
a. is less effective at treating sleep apnea than is uvulopalatopharyngoplasty.
b. results in persistent significant weight loss and improvement in sleep apnea.
c. does not improve metabolic factors such as dylipidemia or diabetes.
d. is associated with serious adverse events, necessitating discontinuation of treatment.

34. In post-PCI patients, PPI use in clopidogrel-treated patients:
a. increased the risk of MACE.
b. decreased the risk of MACE.
c. had no effect upon the risk of MACE.
d. None of the above

Answers: 32. c, 33. b, 34. c

CME Objectives

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville

Dr. Kuritzky is an advisor for Endo, Kowa, Pricara, and Takeda.

Functional Cobalamin Deficiency in Diabetes

Source: Solomon LR. *Diabetes Care* 2011;34:1077-1080.

It has been suggested that as many as 30% of senior citizens have so-called functional cobalamin deficiency (FCD), defined as the presence of elevated metabolites such as methylmalonic acid in the face of ostensibly normal cobalamin levels. Since methylmalonic acid should accumulate primarily in the circumstance of vitamin B12 insufficiency, there appears to be some functional deficiency in cobalamin, manifested as increased levels of methylmalonic acid.

The intersection of diabetes with FCD occurs because previous trials have noted that diabetics comprise up to one-third of subjects experiencing improvements in neuropathic signs with vitamin B12 supplementation, and the vast majority of these subjects (88%) did not have decreased vitamin B12 levels.

To better define the epidemiologic profile of FCD, a retrospective review of patients evaluated for cobalamin deficiency from 1993-2005 characterized levels of cobalamin in relation to methylmalonic acid. Because renal insufficiency is associated with increases in methylmalonic acid, creatinine > 1.4 mg/dL was an exclusion criterion.

Among nondiabetics there was an inverse relationship between methylmalonic acid and cobalamin. Among diabetics, however, increasing cobalamin levels were not associated with decreasing methylmalonic acid, suggesting that there was a relative cobalamin resistance.

Equally noteworthy, neuropathy was much more frequent in persons with elevated methylmalonic acid than without (62% vs 18%) and more than 85% of persons treated with pharmacologic doses of cobalamin experienced improvement in neuropathy.

There is substantial controversy over the existence of functional cobalamin deficiency. Considering that cobalamin supplementation has no known important toxicity, clinicians may wish to re-examine the issue of cobalamin treatment for diabetic subjects with elevated levels of methylmalonic acid, even in the face of normal cobalamin levels. ■

Should Leukotriene Antagonists Have Higher Priority for Asthma Control?

Source: Price D, et al. *N Eng J Med* 2011;364:1695-1707.

Current asthma guidelines suggest that once an asthma patient has progressed to the stage of persistent asthma (even mild-persistent asthma), inhaled corticosteroids (ICS) should be the preferred initial "controller" (maintenance) medication. Nonetheless, comparator trials of leukotriene inhibitors (LKT) with ICS have produced inconsistent findings, sometimes indicating superiority of ICS, but other times suggesting equal efficacy of the two classes. Because concerns about adverse effects of ICS in obstructive airways diseases have persisted for several decades, the absence of similar concerns with LKT agents promotes consideration of how to maximize their positive potential.

Two trials comprise the data reported in this publication. In the first, persons initiating controller therapy for persistent asthma (n = 306) were randomized to either ICS or LKT. In the second trial, asthma subjects who had already received ICS for controller medication but who required advancement of pharmacotherapy (n = 352) were randomized to either LKT or long-acting beta agonist (LABA). The primary outcome was the score on the Mini Asthma Quality of Life Questionnaire at 2 months. Secondary outcomes included the same questionnaire results at 2 years and frequency of asthma exacerbations.

At 2 months, the LKT proved equivalent to ICS as initial therapy, and equivalent to LABA as add-on treatment. At 2 years, although not able to achieve the statistical threshold defining equivalence, the outcomes were very similar. There was no difference in the frequency of exacerbations between LKT and ICS or between LKT and LABA when added to ICS. There was no placebo control in this trial, and the trial was open label. Nevertheless, these data suggest that in a "real world" setting, the efficacy of LKT in asthma may have been underestimated. ■

Selenium Impacts Orbitopathy in Graves Disease

Source: Krassas GE, et al. *N Eng J Med* 2011;364:1920-1931.

Ocular abnormalities associated with Graves disease are sometimes called Graves' orbitopathy (GORB) and occur in as many as half of Graves' disease cases. Treatments for GORB include glucocorticoids and irradiation, but are generally reserved for moderately severe disease. Mild GORB has been shown to spontaneously regress (20%), remain stable/unchanging (65%), or advance (15%). Hence, a safe intervention to prevent advancement of GORB would be desirable. The antioxidant effects of selenium led to consideration of its potential favorable impact upon GORB.

This controlled trial randomized patients (n = 107) to selenium sulfide 100 mcg twice daily or placebo for 6 months. GORB evaluation was done at baseline, 3, 6, and 12 months. The primary outcome was the percentage of patients improving from baseline. The study hypothesis was that active treatment would improve the number of persons with GORB regression by 25%: from 20% (as seen in naturalistic follow-up of untreated GORB) to 45%.

By 6 months, there was a statistically significant improved quality of life and regression of GORB, which was reconfirmed at 12 months. There were no serious adverse effects seen with selenium.

Although it would have been nice to have seen selenium levels before and after treatment, and hopefully a correlation between selenium repletion and outcomes, these preliminary data are still quite supportive of a role for selenium in early GORB. ■

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